Claims 1-2 and 9 are rejected under 35 U.S.C. 103(a) as being unpatenable over WO 98/52565, hereinafter referred to as WO '565, in view of US 6,001,848 hereinafter referred to as US '848 and US 6,444,679.

To review the key features of the present invention, applicant wishes to offer the following:

Claim 1 recites, in part, a method for treating chemical dependency by administering, a combination of a serotonin reuptake inhibitor and a delta opioid receptor of formula I

Claim 2 depends from claim 1 and is readable on the elected species, a delta opioid receptor of formula I.

Claim 9 recites a group of specific serotonin reuptake ligands including sertraline.

WO '565 discloses the treatment of alcohol dependence with a combination of an opioid antagonist and a serotonin reuptake inhibitor. The selected opioid antagonists include, for example, naloxone which is recognized by those skilled in the art as belonging to the mu opioid receptor class. Opioid drugs are known to have selective binding affinity for cellular tissue and are classified as mu (μ), delta (δ) and kappa ($\propto$) receptors.

WO '565 fails to teach or suggest other classes of opioid receptors i.e. delta or kappa are used in combination with a serotonin reuptake inhibitor.

Of particular importance to applicant is the failure of '565 to teach or suggest the use of a delta receptor in combination with a serotonin reuptake inhibitor, the main embodiment of the present invention.

In Examiner's opinion, this deficiency is remedied by reference to US '848 relying on column 7, lines 10-45 and column 26 line 45-60. Applicant is at a loss to find any teaching or suggestion therein that would motivate one skilled in the art to use a delta opioid receptor in combination with another drug to treat chemical dependence.

Applicant asserts that the mere observation in '848 that a particular mu receptor can bind to delta sites at higher dosage does not lead one skilled in the

art from the mu- SSRI combination of '565 to the delta- SSRI combination of the instant invention.

Moreover, the tendency of a drug such as naloxone to lose its selectivity at higher dosages and bind to delta sites was reported in 1979 (see column 26, line 54). Is it Examiner's position that all mu receptors reported since 1979 were in fact also delta receptors or suggested the use of delta receptors?

Applicant believes that a nexus between a specific property or function of naloxone and the use of delta opioids in a combination therapy can only be drawn in hindsight.

The '848 patent discloses the use of an opiodergic compound, such as naloxone, in combination with a serotonin reuptake inhibitors including for example, sertraline. If the observations reported therein regarding increased bonding of naloxone due to chronic ethanol exposure and delta bonding at high dosage do serve to remedy the deficiencies in WO '565; then arguendo, the claims of '565 and '848 read on both mu and delta receptors. In that case, the inventors of '565 and '848 would have rights beyond their claimed invention.

While naloxone has shown interesting binding properties, it is not a delta receptor. Furthermore these binding properties, while noteworthy and of scientific interest, fail to suggest or motivate one to combine known delta opioid receptors, e.g. US 6,503,905 and US 6,444,679, with 5-HT inhibitors to treat chemical dependence.

Double Patenting

Applicant timely files a terminal disclaimer. Please see attached document.

Respectfully submitted,

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